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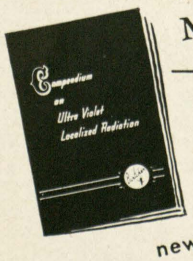

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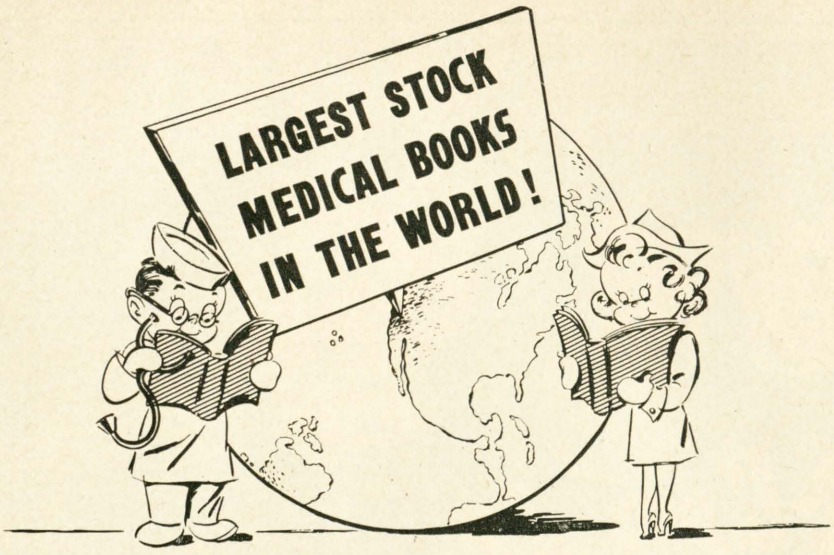

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EDITORIAL

MEDICAL ARTS AND SCIENCES is a journal which deals with science and the application of science in medicine. Art and science are combined inseparably in the practice of medicine, and the *art* and *science* are to some extent synonymous. By necessity, in the past, medical practice has outrun the progress of science. It is no longer necessary, as some still urge, for medical practice to be in advance of, or even independent of, scientific groundwork. Scientific medicine tempered with humanity is the best instrument for the relief of sickness.

Published by the College of Medical Evangelists, a school in which the humanitarian side of medical practice receives foremost emphasis, this journal will contain articles which cover the practical, cultural, and philosophical as well as the experimental, investigative, and critical sides of medicine. In it original studies by members of the faculty as well as the alumni will be given circulation.

MEDICAL ARTS AND SCIENCES

VOLUME 1 APRIL, 1947 NUMBER 1

RELIGION AND HEALTH*

ARTHUR L. BIETZ, Ph.D.

Before we can speak of religious values in health we must clarify the atmosphere around the concept of religion. Every intelligent human being should construct to the best of his ability a philosophy of life. By a philosophy of life we mean an interpretation of life, a view, provisional at least, of the main purpose of life and the undergirding principles by which life must be supported. If we are to cope successfully with the obstacles of life we must have some concept as to how these difficulties should be met before they come.

Every serious philosophy of life involves a positive or negative view toward God and religion. A philosophy of life may be termed a religious philosophy if the view of God holds a central and all-important place. An orientation toward life is nonreligious when some other goal takes the place of first importance in life.

When we think of religion as an adequate philosophy of life, it is easy to see its implications for healthful living. A philosophy of life becomes the dominating principle of thought and of conduct. Life thus has an end, a purpose, an object, toward which it moves. The quest for meaning is one of the basic needs of life. When the quest is frustrated, life itself becomes a meaningless speck on the ocean of uncertainty.

Urgent psychic problems of patients have given impetus to recent advancements in psychosomatic medicine. Medicine is beginning to recognize that it cannot confine itself strictly to the functioning of the physiological organism. Life is unitary; that which occurs in the realm of the psyche also carries its implications to the soma. A former false dualism is now giving way to the present organismic approach to the patient.

To understand a neurosis, or a state of stress, it is necessary to know that its origin and causes are psychic. The cure for such disturbances must therefore deal with psychic implications as well as the organic.

Jung[a] has said: "A psychoneurosis must be understood as the suffering of a human being who has not discovered what life means for him."

If this definition of a psychoneurosis is correct the sufferer is seeking for something which will take possession of him and provide meaning and structure to a confused disorganized state of existence.

In the past clergymen were called upon to minister to people in a confused state of mind. Certain theories of life were almost universally accepted in our culture. The Bible usually provided an organization of life for the framework of culture. Divine revelation was generally conceded. The scientific age, however, has led many to reject former religious concepts. Having cut these former ties, men are not at peace, because life has lost its meaning. Today

* From the Department of Applied Christianity, College of Medical Evangelists.

many patients who would not think of going to clergymen, come to physicians. Therefore not only must the physician of a necessity deal with strictly organic problems but also he is forced into the realm of the patient's philosophy of life. To minister successfully to such patients with a disorganized view of life, the physician himself must have a philosophy of life which will aid his patients in the process of reorganization.

It should be remembered, however, that in the realm of an adequate meaning of life which has religious implications the physician cannot proceed on the same basis that he can in giving the ordinary physical prescriptions. A physician may give a prescription with religious implications, but the problem still remains as to how this "medicine" shall be administered. One thing is certain: it cannot be administered at any time and to any patient as one would administer a pill or so many injections of drugs. It seems unnecessary to say that religious prescriptions without genuine religious convictions on the part of the patient may lead to greater conflicts rather than to a resolution of conflicts which already exist.

Jung[b] makes this observation on the significance of religion: "I should like to call attention to the following facts. During the past thirty years, people from all the civilized countries of the earth have consulted me. I have treated many hundreds of patients, the larger number being Protestants, a smaller number Jews, and not more than five or six believing Catholics. Among all my patients in the second half of life—that is to say over thirty-five—there has not been one whose problem in the last resort was not that of finding a religious outlook on life. It is safe to say that every one of them fell ill because he had lost that which the living religions of every age have given to their followers, and none of them has been really healed who did not regain his religious outlook."

Jung further observes, "It seems to me, that, side by side with the decline of religious life, the neuroses grow noticeably more frequent."

Dunbar[a] says: "In medicine, we find it necessary to consider, not merely the objective environment, but also its subjective counterpart within the organism, which we find in its most integrated form in the Weltanschauung of the individual. . . . Physicians in general . . . are beginning to call attention to the importance of Weltanschauung from a purely practical point of view."

Dr. Dunbar[b] continues her discussion with many quotations from psychiatrists who hold this point of view. She says: "C. M. Campbell has called attention repeatedly to this aspect of our problem, saying that 'the study of "beliefs" is part of the general study of the mechanism of man's adaptation to his environment.' The term, health, is now coming to include sanity of beliefs as well as soundness of body. . . . Man's environment to which he must adjust, includes, not only (a) supplies to acquire, and (b) hostile organisms to fight, but also the spiritual forces of a social environment. . . . Man's beliefs add to the quality of life and give it value, and may also prolong it. . . . Beliefs affect the actual length of life of individuals and groups, and to scrutinize them is the 'most important and the most difficult task in the field of public health.' "

It is now a well-known fact that emotions may disturb physiological functions. When life does not move toward specific goals which are considered worth while by a patient, emotional disturbances are much more likely to occur. Concerning the influence of disturbed emotions upon the functions of the organism, Dr. Dunbar[c] says, "We know now that bodily changes may be brought about by mental stimuli, by emotions, just as effectively as by bacteria and toxins, and that physio-

logical changes accompanying emotion may disturb the function of any organ of the body.

Referring to the prophylactic value of religion, Dr. Sadler says: "No one can appreciate so fully as a doctor the amazingly large percentage of human disease and suffering which is directly traceable to worry, fear, conflict, immorality, dissipation, and ignorance—to unwholesome thinking and unclean living. The sincere acceptance of the principles and teachings of Christ with respect to the life of mental peace and joy, the life of unselfish thought and clean living, would at once wipe out more than half the difficulties, diseases and sorrows of the human race. In other words, more than one half of the present affliction of mankind could be prevented by the tremendous prophylactic power of actually living up to the personal and practical spirit of the real teachings of Christ."

With increasing understanding of the emotional and environmental aspects relating to disease, comes the realization that the patient's outlook on life is highly significant. Emotions result from attitudes. Attitudes constitute a state of readiness to respond and are linked with one's views of life. At this point the relationship of religion and health emerges. A way of life and the direction in which it leads an individual may lead to sickness or health. Religion is primarily concerned with an individual's over-all reactions to life. Man's questions move in two major realms: (1) the realm of sensate knowledge, or so-called scientific facts, and (2) the realm of values. Values are of religious import and transfuse themselves into the optimal functioning of the physical organism. The word *religion* means etymologically a binding together. Religion offers a man the opportunity to bind divergent elements into a meaningful pattern. Religion provides a means whereby life may be uncluttered from meaninglessness. In actual illness the will not to get well, or the desire to die, may be a more potent influence than any medicine which a physician can prescribe, but how shall a patient rally without a meaningful reason?

In this connection it should be said that emphasis needs to be given not only to the intellectual content of religion but also to its emotional significance. The religion which will really minister to good health has a functional significance in the realm of emotional belongingness to the cosmos. Man is a denizen of two worlds simultaneously. He must have a terrestrial as well as a cosmic orientation to life. Wise counsel combined with healthy religious attitudes and beliefs may be of great value in meeting both the need for security and the need for love, which are crying needs in this age of disillusionment. Indeed, it is not wrong to say that the basic problems of this age involve the meaning of life and the reasons for prolonging the struggle.

Concerning the value or contributions of religion to health, Dr. Earl D. Bond says: "There is no integration which compares with that which comes from religious faith or the religious goal."

In the same vein speaks Hadfield: "I am convinced that the Christian religion is one of the most valuable and potent influences that we possess for producing that harmony and peace of mind . . . needed to bring health and power to a large proportion of nervous patients."

Dr. Harlow Brooks writes: "The spiritual side of the case must not be neglected in this disease [angina pectoris] in which emotions play so important a role. The developments of a philosophy of life, of the power of adaptation of desire to possibilities, the cultivation of suitable hobbies of a restful character, are of real medical benefit."

Strecker says: "It is not an overstatement to say that fully 50 per cent of the problems of the acute states of an illness and 75 per cent

of the difficulties of convalescence have their primary origin not in the body, but in the mind, of the patient."

From these foregoing statements we are safe in saying that there is no such thing as a purely organic illness. It is also hard to conceive of a purely psychic illness unaccompanied by organic stress. In every illness there is a living experience in the whole organism which is significant only because the psychic and the somatic are united in a living unitary movement.

The true medical practitioner must practice not only with an analytical head but also with a sympathetic heart which has found its home in the universe. Religion binds together and synthesizes. Medicine must pass from purely analytical procedures to those of synthesis which move in the realm of values. John G. Sinclair has written thus in his "Heart or Head."

> "Tell me how is beauty read
> To best advantage? By the heart
> Which ahs and sighs and will not part
> Or by the analytic head?
>
> Heart, possessive, seeks essentials,
> Feels reciprocal dependence,
> Waives sartorial resplendence,
> Gives but cannot be impartial.
>
> Head, aware, through symbol logic
> Unifies its world of objects,
> Stars and atoms in its projects,
> Guides electro-mass panurgic.
>
> Heart when headless pants for breath
> Head when heartless conjures death."

The analytical, mechanistic medic may conjure death, whereas the practioner who takes into consideration a combination of the heart and head will make for a far better prognosis.

There are three fundamental entities with which we must reckon in the universe: matter, energy, and life. To deal only with matter and energy is to leave the most important element untouched. There is a vitalistic principle in the organism which defies scientific analysis. Life adds to the matter-energy combination the power to observe, to think, to convert thought into action. Matter and energy alone do not make up a patient. There is much more to life than can be comprehended in energy or matter. Life moves in harmony with a predetermined complex plan even as physical laws operate in the realm of energy and matter. An exploration of the laws of life will yield large results. These laws are understood and seen in the realm of religious values which are not fully discerned by sensate procedures.

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A NEW SURGICAL APPROACH

FOR VAGOTOMY, DIAPHRAGMATIC HERNIOTOMY, SPLENECTOMY, AND OPERATIONS UPON THE GASTROESOPHAGEAL AREA THROUGH THE LEFT SUBDIAPHRAGMATIC EXTRAPERITONEAL SPACE*

A PRELIMINARY ANATOMICAL STUDY

H. A. DAVIS, M.D.

INTRODUCTION

Surgical operations upon structures lying immediately beneath the left side of the diaphragm frequently are technically difficult because of inadequate exposure. Such operations include resection of the cardiac portion of the stomach with esophagogastro anastomosis, splenectomy in the presence of dense adhesions between the spleen and the parietal peritoneum, resection of the body and tail of the pancreas and the repair of diaphragmatic hernia and eventration. Recently, as a result of the work of Dragstedt, resection of both vagus nerves has been advocated for the treatment of gastroduodenal ulceration. This procedure may be performed through the thorax or through the peritoneum.

The transperitoneal approach possesses the advantage of enabling the surgeon to examine the stomach and duodenum and to do, if necessary, a gastro-enterostomy in addition to the vagotomy. It has, however, the definite disadvantage that if the patient has been subjected previously to gastroduodenal surgery, adhesions in the upper abdomen will render exposure of the vagus nerves both difficult and hazardous. In the transthoracic approach, on the other hand, the pleural cavity must be opened.

In a recent report Grimson described thoracic complications following transthoracic vagotomy. In 5 of 33 patients postoperative pneumonia occurred. All 33 patients presented a pleural effusion on the side of the thoracotomy, and in 3 the fluid accumulation was great enough to cause a shift of the mediastinum. Atelectasis of the left lung was noted in 5 patients on X-ray examination. The experience of Grimson has been confirmed by others who have used the transthoracic approach. In addition, many of these patients subsequently complain of pain in the left side of the chest in the line of the incision, which is probably due to injury or involvement of the intercostal nerve at the wound site.

These considerations induced us to investigate by anatomical studies the possibility of devising a new surgical approach which would possess none of the disadvantages of the transthoracic and transperitoneal approaches. By using the approach through the left subdiaphragmatic extraperitoneal space, we discovered that not only was it possible to expose the vagus nerves at the lower end of the esophagus but that it was also technically feasible to carry our surgical procedures upon the diaphragm, the splenic artery and vein, the spleen, the body and tail of the pancreas, and the cardio-esophageal junction through the same incision.

* From the Department of Surgery and the Graduate School of Medicine, College of Medical Evangelists.

The purpose of this paper is to present a preliminary anatomical study of the left subdiaphragmatic extraperitoneal space and to describe briefly the technic of certain surgical operations carried out through this approach.

ANATOMY OF THE LEFT SUBDIAPHRAGMATIC EXTRAPERITONEAL SPACE

The left subdiaphragmatic extraperitoneal space is, of course, a potential rather than an actual space. It lies between the parietal peritoneum in front and Gerota's fascia behind, and extends downward from the dome of the diaphragm to the lowest point of attachment posteriorly of the left leaf of the diaphragm. The shape of the space is irregular, having on cross section the appearance of a truncated cone, which is funnel-shaped, with the narrow end superior and the broad end inferior.

The contents of the space are of interest. It contains fatty and areolar tissues in which are imbedded blood vessels, nerves, the left kidney, the left suprarenal gland, the tail and part of the body of the pancreas, and the upper part of the descending colon. The blood vessels are the left renal artery and vein, the suprarenal vessels, the splenic artery and vein, the inferior phrenic artery (left), and the celiac artery. In the upper and innermost

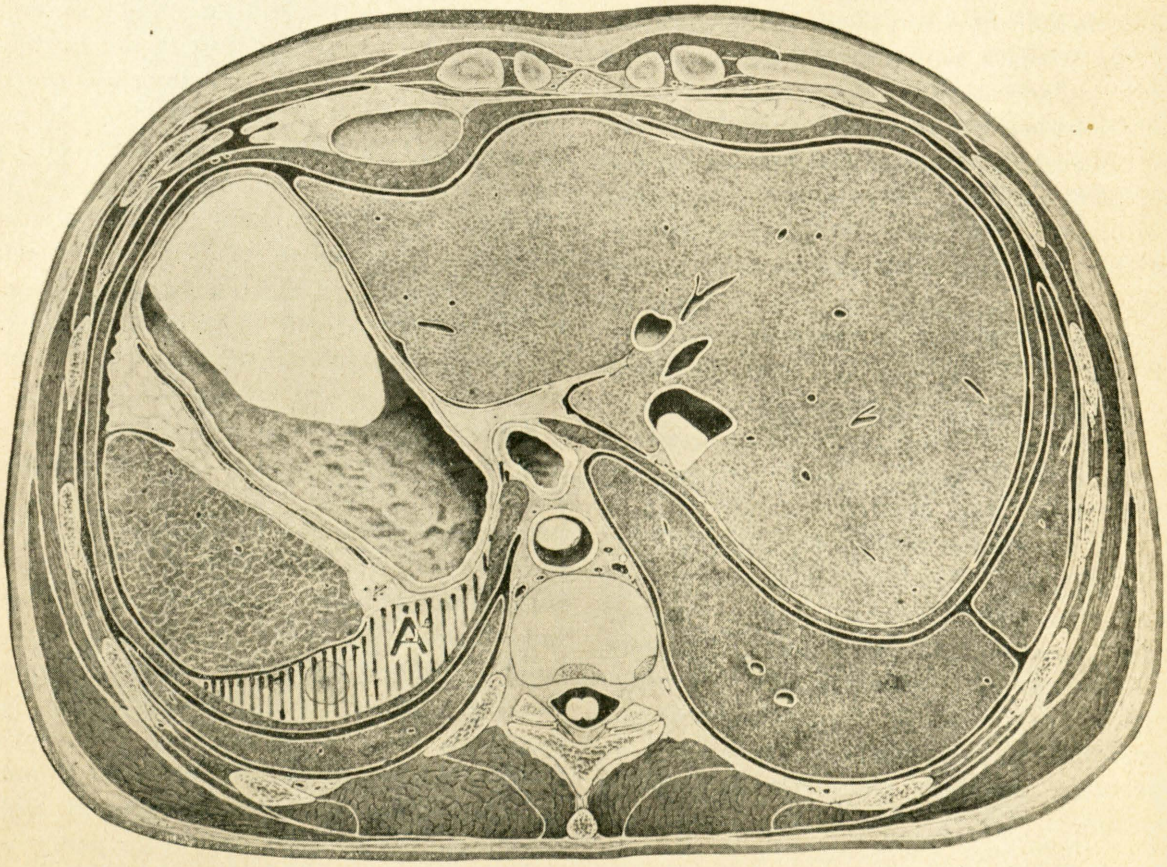

Fig. 1.—Cross-section through upper part of left subdiaphragmatic space. (Shaded area marked A.)
(Modified from Eycleshymer, A.C., and Shoemaker, D.M.: A Cross-section Anatomy, p. 71, D. Appleton and Company, New York, 1923.)

portion of the space is found the esophagus as it passes through the esophageal hiatus of the diaphragm at the level of the 10th thoracic vertebra (figure 1).

The relations of the left subdiaphragmatic extraperitoneal space are:

(a) Upper anterior—the parietal peritoneum, the cardiac portion of the stomach, the esophagus, the spleen, and the left lobe of the liver.

(b) Middle anterior—the parietal peritoneum, the stomach, the liver, the left side of the colon, and the spleen.

(c) Lower anterior—the parietal peritoneum, the stomach, the liver, the colon, and the jejunum.

(d) Posterior—the diaphragm, the pleural cavity, the inferior tip of the left lung, the 10th, 11th, and 12th ribs, Gerota's fascia, the latissimus dorsi, and the serratus posterior inferior muscle.

(e) Lateral—the spleen, the diaphragm, the pleural cavity, the inferior tip of the left lung, the 7th, 8th, 9th, 10th, and 11th ribs, the intercostal muscles, the latissimus dorsi, and the external and internal oblique muscles.

(f) Medial—the esophagus, the aorta, the diaphragm, the pleural cavity, the inferior tip of the left lung, and the bodies of the vertebrae.

THE SURGICAL APPROACH

The skin incision is shaped like a hockey stick. The 12th rib on the left side is carefully palpated, and an incision is made starting 1 inch above the junction of the 12th rib with the transverse process and extending over the 12th rib to a point 1 or 2 inches beyond its tip. The incision is deepened so as to expose the latissimus dorsi muscle and the sacrospinalis sheath. The latissimus dorsi muscle is incised, exposing the 12th rib. The serratus posterior inferior and part of the external and internal oblique and transversus abdominis muscles are divided in the line of the incision. The sheath of the sacrospinalis muscle is opened and the muscle is retracted medially. This provides a more adequate exposure of the 12th rib close to the transverse process. The periosteum over the 12th rib is incised and the rib is resected subperiosteally. It is important that the rib be divided at the transverse process, in order that sufficient exposure of the "space" be provided. The 12th intercostal vessels and nerve will now be seen. The subcostal ligament should be divided, since this will permit the retraction upward of the intercostal vessels and nerve and the periosteal bed of the rib. The ilio-inguinal and iliohypogastric nerves will be observed lying more inferiorly and should be avoided. The fascia of Gerota, or the perirenal fat capsule, is incised over the perirenal fat in a line lying at the level of the spinous process of the 1st lumbar vertebra. In this way it is possible to avoid entering the pleura. It is to be remembered that the pleural reflection extends to or slightly below the 12th rib. After Gerota's fascia has been opened, the left subdiaphragmatic extraperitoneal space is entered.

THE TECHNIC OF VAGOTOMY

The left subdiaphragmatic extraperitoneal space is entered in the manner which has been described. Following division of the fascia of Gerota, the fingers of the right hand are introduced between the left kidney and the diaphragm, and the kidney with the left suprarenal gland is gently retracted laterally. The fingers of the hand are now passed along the medial leaf of the diaphragm, and encounter the peritoneum, which is carefully stripped from the diaphragm from above downward and from the medial to the lateral aspects of the posterior portion of the diaphragm. In this manner the intraperitoneal contents which occupied the superior portion of the

left subdiaphragmatic space are displaced downward. These contents include the cardiac portion of the stomach, the spleen, and the body and tail of the pancreas. In this way the esophageal hiatus of the diaphragm can be visualized and palpated.

The exposure is considerably enhanced by retracting the tissues with Balfour and Deaver retractors. Retraction downward and outward of the peritoneum and its contents will permit the surgeon to see readily the cardiac portion of the stomach and the esophagus just prior to its passage through the diaphragmatic hiatus into the mediastinum. By blunt dissection the esophagus immediately above the stomach can be mobilized and drawn downward into operative field. The vagus nerves are palpable as cordlike structures on each side of the esophagus and can be readily resected.

After completion of the operative procedure the peritoneum with its contents is replaced. The opening in Gerota's fascia is closed with a continuous suture. Interrupted sutures are used to close the opening in the sacrospinalis fascia, to approximate the divided muscles, the subcutaneous fat, and the skin.

THE TECHNIC OF DIAPHRAGMATIC HERNIOTOMY

Since most instances of diaphragmatic hernia and diaphragmatic eventration occur in the region of the esophageal hiatus of the diaphragm, the same exposure is used as for vagotomy. After the peritoneum and its contents have been stripped away, the diaphragm is well visualized and is easily accessible for the performance of various surgical procedures.

THE TECHNIC OF OPERATIONS UPON THE CARDIOESOPHAGEAL AREA

The same exposure is used as for vagotomy. If such procedures are to be done as Heller's cardiomyotomy, the Heyrovsky-Grondahl esophagogastrostomy, or resection of the cardiac portion of the stomach followed by anastomosis between the esophagus and stomach, the peritoneum should be opened and the stomach exposed. A strip of umbilical tape is passed around the esophagus at its junction with the stomach. The esophagus is mobilized from the edge of the hiatus in the diaphragm by means of the right index finger. The operations enumerated above are carried out in the usual manner. The anastomosis of the esophagus to the stomach may be kept extraperitoneal by suturing the edges of the opening in the peritoneum to the stomach wall below the anastomotic site. In the event that a leak occurs at the suture line, the escaping fluid will enter the subdiaphragmatic extraperitoneal space, from which it can be readily evacuated by external drainage. This provides an extra safeguard against postoperative peritonitis. The details of this procedure will be described in a subsequent paper.

THE TECHNIC OF SPLENECTOMY

Through this approach it is possible to perform a splenectomy. After incision of the fascia of Gerota, the left kidney and suprarenal gland are retracted medially toward the spine. The peritoneum is stripped from the diaphragm laterally. The peritoneal cavity in the region of the spleen is entered by incision of the parietal peritoneum, and the extent of the perisplenic adhesions is determined. The splenic artery and splenic vein may be ligated before the spleen is exposed. In this way the blood supply to the spleen is controlled at the outset of the operation. When the spleen is surrounded by dense adhesions, exposure of the vascular pedicle may be very difficult.

The approach to splenectomy which has been described here renders it unnecessary to separate the dense adhesions between the

spleen and peritoneum, because after control of hemorrhage by ligation of the splenic artery and vein, the spleen, with its adhesions and the surrounding parietal peritoneum, can be removed in one mass. When this is done, the opening in the peritoneum is closed with a continuous suture.

Finally, the tail and part of the body of the pancreas are easily palpated through the same approach, which may be used for exploration and resection of this part of the pancreas.

CONCLUSIONS AND SUMMARY

In this paper are presented anatomical studies carried out in the cadaver on the left subdiaphragmatic extraperitoneal space.

The anatomy of the space is discussed, and it is pointed out that the space lies between Gerota's fascia and the parietal peritoneum, and has an irregular funnellike shape whose narrow end lies superiorly at the esophageal hiatus and whose broad end is inferior.

The space is approached through an incision over the left 12th rib, which is resected subperiosteally.

It is possible to expose through this space the cardiac portion of the stomach, the lower end of the esophagus, both vagus nerves, the diaphragm, the tail and part of the body of the pancreas, the splenic vessels, the spleen, and the colon.

The surgical approach through the left subdiaphragmatic space has the advantage of being both extrapleural and extraperitoneal.

It should be emphasized that no major blood vessels are encountered in exposing these structures through this space.

It is suggested on the basis of these anatomical studies that this approach may be utilized for vagotomy, for splenectomy, and for operations upon the diaphragm, the cardio-esophageal junction, the body and tail of the pancreas.

I wish to take this opportunity of thanking Dr. R. M. Andrews and Dr. E. T. Smith for their assistance in carrying out certain of these dissections.

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CEREBRAL ANOXIA AND ITS RESIDUALS*

I. HISTORICAL INTRODUCTION

CYRIL B. COURVILLE, M.D.

From the time of Aristotle (384-322 B.C.), who believed that man could not live on Mount Olympus because "he could not respire in that air, otherwise too thin for respiration," to our present "air age," when we are beginning to understand something of cerebral anoxia, stretches the long history of the effects of oxygen want on the human organism. To be sure, it is very doubtful whether Aristotle had any very clear concept of the place of oxygen in the body economy, but it is remarkable that, for his day, he considered the "too thin" air to be the cause of the phenomenon which is now called mountain sickness. It is also very doubtful that with all our increase in knowledge as to the mechanism and effects of anoxia on the brain, we yet fully appreciate all the ramifications of the problem. Therefore to this very old, yet very new subject, we may profitably turn our attention.

But before getting too deep into the historic lore dealing with anoxemia, or *de suffocatione,* as our professional forebears called it, a brief statement of its various causes is in order. Today we recognize that there are many ways in which the cells and tissues of the body may be deprived of their oxygen supply. There may be too little oxygen in the inspired air, fumes, or in the gases used for anesthetic purposes. Mechanical obstruction of the air passages may cause sudden and profound asphyxia by excluding air from the lungs. Pneumonia may interfere with the interchange of oxygen and carbon dioxide through the alveolar walls. Slowing of the blood stream (stagnation) may lessen the amount of oxygen available to the tissues in a given length of time. Heart failure, even though temporary, may be followed by irreparable brain damage on this basis. Interference with the oxygen-carrying capacity of the hemoglobin, as in the formation of methemoglobin, may likewise result in death, immediate or delayed, or in neurologic residuals of varying degrees of severity. The history of these various clinical conditions which may result in brain damage has, of course, started from widely divergent points in the centuries past, all approaching a modern focus in the pathology of the ultimate cerebral lesion. Only recently has medicine come to recognize in any full sense the nature and mechanism of brain damage due to oxygen lack. In spite of its kaleidoscopic aspects, the story of anoxia proves to be unusually interesting, and a brief survey of its salient features will serve us well as a point of departure for an investigation of its causes and effects.

THE NOXIOUS GASES OF MINES

Mining is as old as the various civilizations whose very existence was dependent upon its development. The demand for both common and precious metals increased progressively as time went on. Although it is uncertain how soon men became aware of the dangers of asphyxiation, this must have become evident very early to the ancient Egyptians, whose mine galleries, according to Diodorus (4th century B.C.), were narrow and low, and were

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without ventilation. The same applies to the silver-lead mines of ancient Greece, which had already been worked for "many generations" at the time of Xenophon (430-355 B.C.). The shafts were deep, the passages crooked and narrow, and though ventilation was attempted

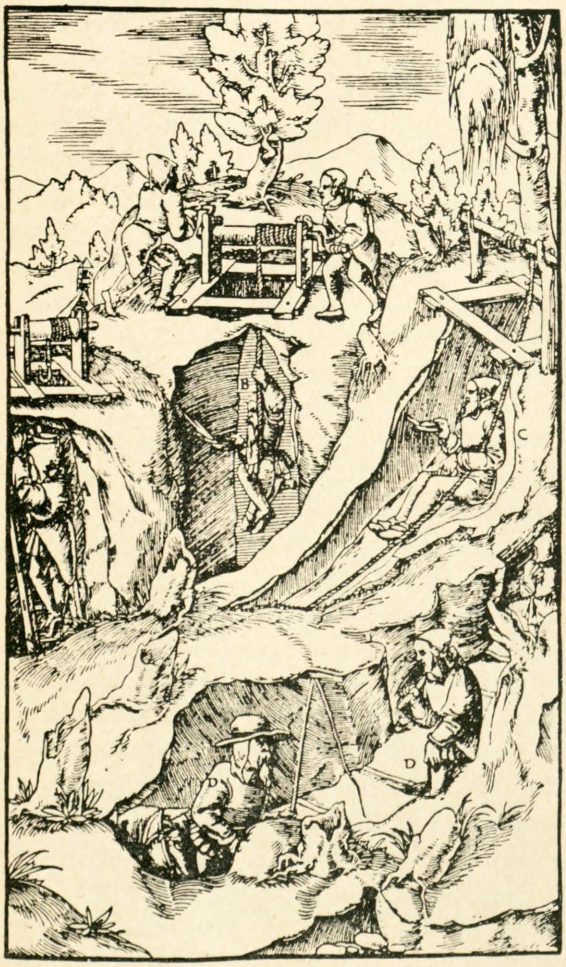


Fig. 1.—Mining operations in the Middle Ages. The use of oil lamps as detectors of asphyxiating gas as well as a source of light is suggested in this woodcut from *De re metallica* (1556.)

by means of fires, the atmosphere must have been very foul (Rickard, 1932).

It was in the time of the Romans, however, that mining was pushed to the limit of men and materiéle. In some mines the galleries were extremely deep and long. Vitruvius (a contemporary of Christ) was perhaps the first to mention the fact that death might follow inhalation of noxious vapors, and advocated the use of a lighted lamp, which was let down into the shaft. If the lamp continued to burn, the miner could descend with safety. Galen (A.D. 131-201) is thought to have been the first physician to call attention to the suffocating effects of fumes so evident, for example, in the copper sulphate mines of Cyprus.

For many centuries apparently little more than this was learned about the asphyxiating gases incident to mining, for we find that Agricola in his famous *De re metallica* (1556) again called attention to noxious gases in mines and mentioned difficulties in respiration, headaches, or actual suffocation resulting therefrom. His illustration of miners descending into pits with their lamps before them suggests their use as a detector of the presence of noxious gases (figure 1). Although others, including Ramazzini (1746),* had something to say regarding noxious gases and their effects, it is difficult to distinguish in their writings the asphyxial effects of these gases from the metallic poisonings incident to inhalation of vapors.

Throughout the sixteenth and seventeenth centuries the situation did not change. It was not until the demand for coal as fuel became acute in the industrial period of the nineteenth century that the problem of asphyxia by mine gas became a vital problem. It then came to be recognized that the presence of blackdamp, or chokedamp (carbon dioxide and nitrogen), and of firedamp (methane) was a source of danger by suffocation.

The asphyxiating effect of carbon monoxide as experienced in the coal mines of the nine-

* It is tempting to read the cerebral effects of asphyxia into the following quotation translated from Ramazzini: "[The lungs] suck in the mineral spirits along with the air, and so receive the first injury; after which the same spirits, admitted within the course of the circulation and mingled with the blood, corrupt and taint the natural temperament of the brain and nervous juice, from which spring the tremblings, stupidity, and other disorders above mentioned." It is to be concluded rather that these symptoms are the nervous effects of metallic poisoning.

teenth century is now seen in the fuel gases and automobile exhausts of the twentieth century. Although this story is as yet but recent history, it is worth while mentioning the extensive investigative work on this subject of Barcroft and Haldane in England and Henderson and Haggard in this country. The efforts of these workers have not only served to clear up many of the problems in respiration but have also contributed much to the prevention of asphyxiation and its evil effects by pointing out sources of danger.

But a scant half century after Agricola (1556) recorded his observations on the asphyxial effects of mine gases, men on the other side of the world were beginning to experience another type of anoxemia which manifested itself as "mountain sickness." The history of this type of oxygen want has almost as interesting a history.

"MAL DE MONTAGNES"

Just when "mountain sickness" first came to be appreciated is uncertain. But it does seem clear that in the time of Aristotle (384-322 B.C.) it was already appreciated that man experienced difficulty in breathing in high altitudes. It may have been this unpleasantness as well as their superstitions that served as a deterrent to those more adventuresome individuals who might otherwise be interested in exploring the higher reaches of the mountains. However, it may well be believed that in the fastnesses of the Himalayas and the Andes men at this period had already come to accept the rarefied atmospheres of their homelands at its face value.

Be all this as it may, the fact remains that it was the European, with his tendency to record his experiences, who was the first to make note of this mysterious malady which dogged the steps of the adventuresome mountain climber. Close on the heels of the conquistadors, who had the effrontery to assail the empire of the Incas with a handful of mounted men with firearms, came the emissaries of the Catholic Church, who evidently had more time than the soldiers to analyze their physical experiences and record them. In 1588 the Jesuit, Joseph de Acosta,* very vividly described the acute symptoms experienced by himself and fellow travelers in the Andes, which report is still one of the classics of medicine (Major, 1932). He attributed the difficulty in breathing, the lack of energy, and the more disturbing nausea to a "subtile and delicate" element of the air, "that is not proportional with the breathing of man, which requires a more grosse and temperate aire." Within the next century after the first edition of Acosta's book was printed (1588), other travelers in the mountains reported similar experiences. The scientists of the seventeenth and eighteenth centuries (among whom may be named Pascal [1647] and Périer [1648]) explained the symptoms of mountain sickness more or less completely on a mechanical basis (Langley, 1943).

There were others who subsequently experienced discomforts of variable degree while climbing mountains, but it was more than 150 years later that Bouger (1744) accounted for mountain sickness by the labored breathing which occurred at high altitudes. A more correct conclusion (among many suggested possibilities) was reached by Saussure (1803) on the basis of his experiences in the Alps, when he stated that the untoward symptoms of mountain sickness—palpitation, dyspnea, muscular weakness, nausea, and even vomiting†—were the result of a depletion of the

* Acosta, however, was not the first to leave a record of the disturbing symptoms of high altitudes. Jourdanet (1875), who has made an excellent comprehensive review of the problem of mountain sickness, points out that Ordaz, one of the officers in Cortes' force invading Mexico, climbed the mountains around Mexico City only to succumb to fatigue and syncope. Jourdanet states that this is the first time that this condition was called *mal de montagnes*.

† The present writer can testify, as can many other amateur mountain climbers of the West, of the forced respirations, the pounding heart, and the extreme muscle fatigue in a rapid climb even to an altitude of 11,485 feet (Mount San Gorgonio). Mount Whitney (14,501) will try even the muscle-hardened sportsman.

blood of its "phlogiston." This concept was first definitely stated, however, by Clissola (1823), who concluded that debility in mountain climbers was due to a reduction in the amount of oxygen in the atmosphere.

In spite of all this, many conflicting and contradictory theories came to be propounded in the next few decades, most of which were based on the concept that oxygen consumption was purely a physical problem (Payerne, 1851). It remained for Jourdanet (1861) to point out that this was not the case, but rather that the volume of oxygen in the blood was due to its chemical affinity to the elements in the blood stream. This work of Jourdanet and the experiences of contemporary balloonists led Paul Bert (1878) to settle the question by intensive experimentation.

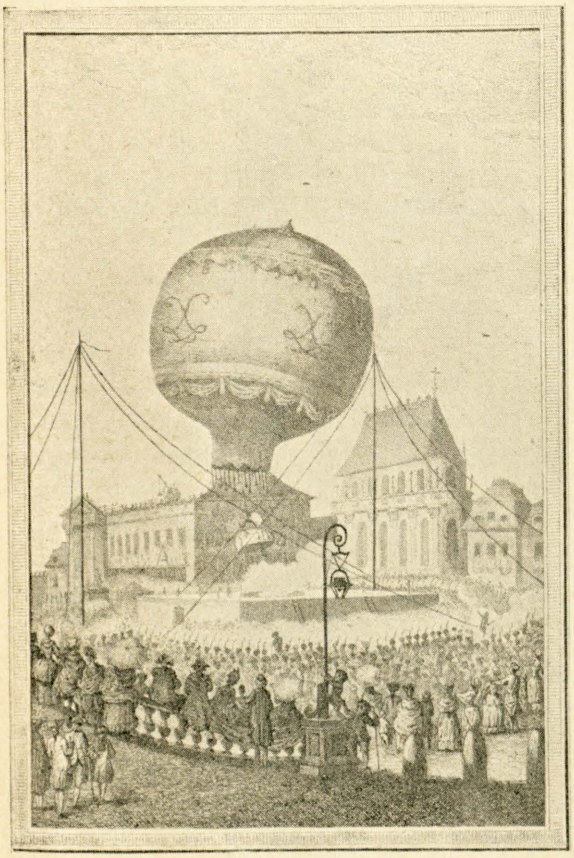


Fig. 2.—The first balloon ascension in 1783. This balloon, constructed by the brothers Montgolfier, carried no human passengers.

A word is in order about the place occupied by balloonists in the discovery of facts regarding the effects of altitude in the production of anoxemia. In 1783 the brothers Montgolfier demonstrated the behavior of lighter-than-air balloons (figure 2). Within four months men began to ascend in these balloons. Although experimentation of barometric pressures and air analysis began within a year (1784), it was twenty years later that any great altitude was reached in this way. In 1804 a French balloonist by the name of Robertson attained the altitude of 26,000 feet and experienced definite symptoms of oxygen want. The same year Gay-Lussac reached an altitude of 23,000 feet, without any great degree of discomfort, however.

There was a lapse of over fifty years (1862) until Glaisher and Coxwell made an ascent for scientific purposes, alleging to have reached an altitude of 29,000 feet. (This was subsequently disputed.) At this height both men experienced disturbances of sight and hearing, and Glaisher became unconscious. Coxwell found himself unable to use his arms and was obliged to pull the valve rope with his teeth, thus saving their lives.

Paul Bert became enthusiastic about barometric pressure, and in 1875 persuaded three fellow scientists—Sivel, Crocé-Spinelli and Tissandier—to undertake a balloon ascension prepared to study the variation of barometric pressure at successive altitudes. At high altitudes these men experienced palpitation, muscular weakness, and somnolence, which preceded loss of consciousness. The balloon acended to an altitude of 28,200 feet, and then began to descend of its own accord. When the balloon reached the ground, Crocé-Spinelli and Sivel were found to be dead, presenting all the hideous aspects of advanced asphyxia, including hemorrhage from the nose and

mouth. Tissandier, though unconscious, escaped with his life.

It was three years later that Paul Bert (1878) published his memorable monograph on barometric pressure, which shed much light on the problems that had disturbed scientists for more than two centuries. His work was accomplished with the use of a specially constructed decompression chamber which duplicated conditions in the higher altitudes (figure 3).

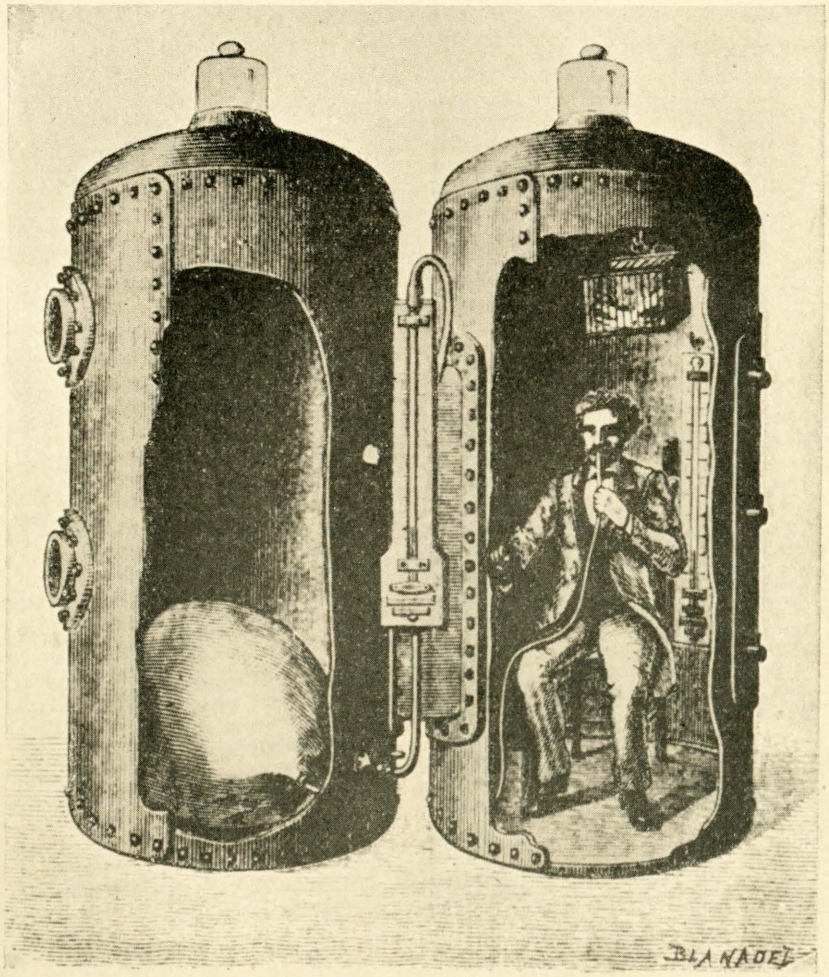


Fig. 3.—Decompression chamber used by Paul Bert in reproducing barometric pressure conditions experienced at high altitudes.

It remained for investigators in our country—Douglas, Haldane, Henderson, and Schneider (1812), who conducted their experiments on Pikes Peak, and Barcroft of England (1925), who studied the effects of altitude in the Teneriffe Mountains of Africa—to write still later chapters in this long search for the cause of mountain sickness.

Coming somewhat as an anticlimax to these observations are the recent findings of Monge (1943) in the identical setting of De Acosta —the Andes. After a lapse of almost three and a half centuries, Monge found that in addition to the acute form of mountain sickness there is a subacute and chronic form

(*soroche* is the Quechua Indian word for it), which are now recognized to be true medical entities.

Still another chapter in the history of the effects of altitude has just been written by the aviators and their medical associates during the recent conflict, but the ink on these pages is still too wet for the facts to be available for scrutiny. No doubt there will be found many counterparts of the 1862 tragedy of Sivel and Crocé-Spinelli when the truth is known.

"DE SUFFOCATIONE"

The lethal effects of asphyxia, or suffocation, as the ancients described it, have been known since time immemorial, and man in his inhumanity to man has taken advantage of this knowledge to do away with his enemies. Infanticide was often accomplished in the same way. Condemned prisoners were dispatched by the less refined method of garroting, or slow strangulation, a method that was not infrequently resorted to in the Spanish Inquisition (figure 4). During the recent war Hitler revived this method of capital punishment to deal with some of his personal enemies.

But in its broader aspects we must look into some features of the history of *de suffocatione*, as it was described when Latin was the language of science. Perhaps the first form of suffocation to be recognized was that of drowning, and the Greeks and Romans at least (being close to the sea) apparently recognized that death by this means was the result of interference with the function of respiration. Celsus and Pliny, for example, were well aware of the possibility of death by suffocation in this way. Galen is credited as first using the term *apnea* to describe cessation of respiration. But only when publication of medical treatises came into vogue could any definite concept of this form of asphyxia come to be widely known. Ambroise Paré, Donatus, and others did describe cases of suffocation by drowning. By this time (as will be shown in a succeeding section) the danger of suffocation by mine gases was already known.

As an example of the status of the question in the seventeenth century we have the comments of John Schenk (1644), who discussed in his large medical treatise something of the early history of suffocation, notably among the Romans. He mentions in particular asphyxia incident to strangulation, drowning, fainting, and from noxious fumes.

Fig. 4.—Asphyxiation by strangling (garrotting) used in the Spanish Inquisition. After an etching by Goya.

Some thirty-five years later Bonet (1679) published his memorable treatise on pathology and also gave an excellent survey of the more recent history of suffocation, mentioning the reports of Platter (1614), Riolan (1649), Bar-

tholin (1654), Richard Lower (1669), and Wepfer (1724). His discussion of *de suffocatione* is chiefly of medical interest, because he was concerned with those diseases of the heart and lungs which may be associated with, or the cause of, this condition. Morgagni (1766), who started out to write an appendix to Bonet's work but who succeeded in writing a long four-volume treatise of his own on "the seats and causes of disease," also reported a number of cases of suffocation chiefly from a medical viewpoint.

By this time this subject had become one of widespread interest, and a number of tracts, monographs, and reports appeared (Shiller [1753]; Mendel [1776]) to enlighten contemporary physicians. These treatises were concerned with asphyxiation incident to the fumes of liquor, of burning charcoal, and of noxious gas of other types, to drowning, and to those episodes which occur at birth. The last group of contributions is of sufficient interest to be given special attention in a subsequent section; the others will here receive brief mention.

We find that Storcke (1705) published an essay on the asphyxial effects of recently fermented liquor. Similarly, Tannenberg (1729) described instances of "suffocation" following exposure to the vapors of fermenting *musto*. Although it is doubtful that many serious asphyxial accidents occurred on this basis, these contributions give one an interesting sidelight on the subject under consideration.

Exposure to noxious or foul-smelling gases from mines, burning charcoal, or decaying organic materials apparently often resulted in asphyxia. This phase of suffocation was the subject of a monograph by Portal (1775), a book which went through at least six editions and which was translated into German. Portal (1796) also published a book of instruction on the treatment of asphyxia from various causes, including mine gases, which was widely read. A contemporary, Carminatus (1777), published an interesting study on the suffocating effects of decaying animal matter.

Another designation which came to have common use in these cases of asphyxia was *de suspensa respiratione,* or suspended respiration (Adams, 1796). This term was often utilized to describe drowning in the several monographs on this subject which appeared about this time (Engelmann [1787]; Coleman [1791]; L'Hermitte [1812]; Chevillotte [1816]).

It is pertinent to point out that the introduction of experimentation played an important role in the development of our knowledge of asphyxia. The introduction of the air pump by Torricelli and Guéricke had made possible experimentation with the variations in air pressure. Sir Humphrey Davy (1800) and others had utilized the experimental method in their work on the physics and chemistry of air, a subject which will receive more specific mention in a subsequent section.

But from the standpoint of asphyxia in its relation to medicine very little had been done in an experimental way until the time of Goodwyn (1788), whose experimental study on "the effects of submersion, strangulation, and several kinds of noxious airs on living animals; with an account of the nature of the disease they produce" is indeed noteworthy. Moreover, the study by Kay (1834) on the physiology, pathology and treatment of asphyxia "in newborn children, and from drowning, hanging, wounds of the chest, mechanical obstruction of the air passages, respiration of gases" represents an effort to apply the experimental method to the problems of asphyxia in man.

At any rate these problems overflowed their medical confines and gripped the imagination of the laity as well. This is so well portrayed in the painting by Thomas Wright reproduced herewith (figure 5).

In the first half of the nineteenth century a bevy of monographs and articles on the subject of asphyxia came into print.* This was made possible by the considerable number of new medical journals which came to be published in the various European countries. Of the various phases of the subject then considered, none attracted quite so much attention as asphyxia of the newborn. To this feature brief attention will be given.

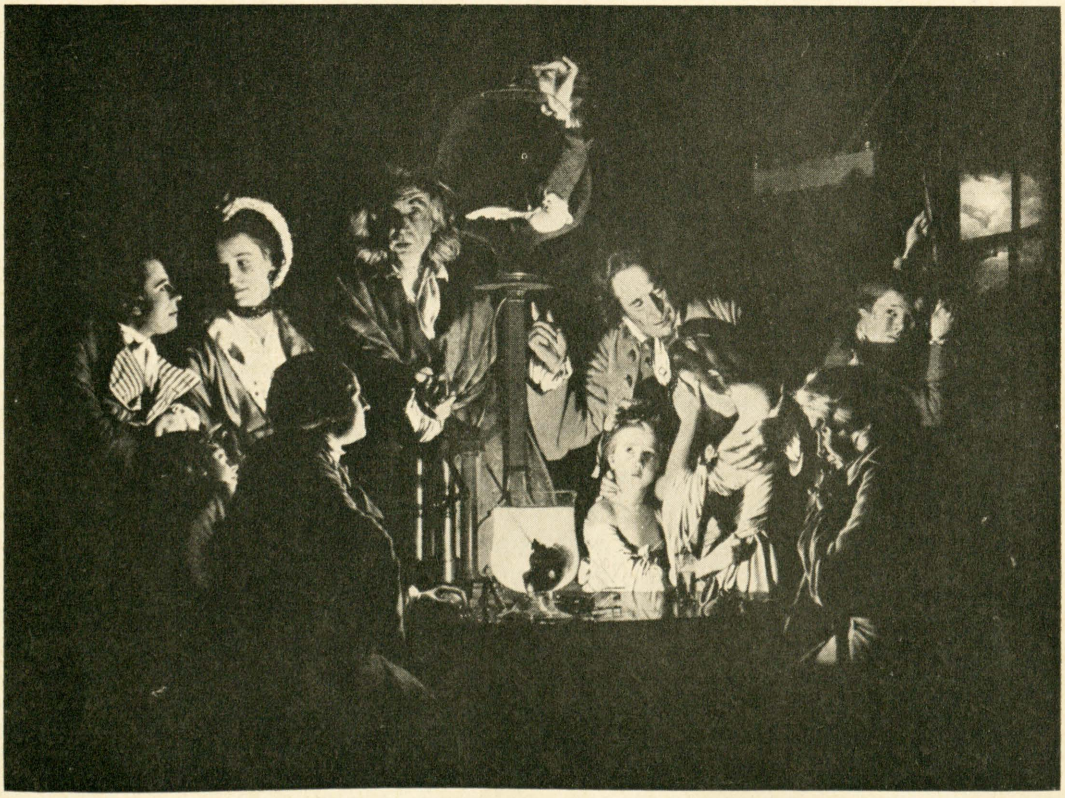


Fig. 5.—*An Experiment With the Air-Pump.* Oil painting by Thomas Wright now in the National Gallery, London. This picture suggests the grip on popular fancy of animal experimentation with lowered oxygen tensions.

"ASPHYXIA NEOPHYTORUM"

The fact that infants are sometimes born dead or die soon after birth has obviously been known since time out of mind. It is very evident from the silence of earlier available literature that this disaster occurred so often as to be commonplace and scarcely worth mentioning. The question of primary interest in this connection is to determine when this situation was recognized to be due to "suffocation." And the answer to this question cannot be given exactly. From available sources it appears that medical interest in the problem developed concurrently with the eighteenth century, and the general interest was followed

* In the Index of the Surgeon General's Library there are to be found titles of 100 monographs dealing with asphyxia (including the neonatal variety) which appeared between 1800 and 1850. In the same period 132 articles appeared in medical literature. It is obvious that between 1775 and 1850 there was an awakening of a remarkable interest in the subject of asphyxia in its various aspects.

specifically by attention to asphyxia in the newborn. This condition was described by a variety of terms: suffocation in the newborn (Roederer [1760]); asphyxia neophytorum (Ehrhart [1785]); asphyxia neonatorum (Regnier [1789]); apparent death in newborn Löfler [1792]), all of which terms are accurately descriptive.

In this particular field several names stand out as pre-eminent. Roederer (1760) was one of the outstanding physicians of this period who had given much attention to the ailments of children. It is therefore pertinent that he be one of the first to write on suffocation in infants. Ehrhart (1785, 1789) was also one of the earliest monographers on asphyxia of the newborn. Regnier (1789), de Waldkirch (1793), and Roose (1794) also wrote treatises on the subject.

After the turn of the nineteenth century the contemporary literature was marked by many contributions to the subject of asphyxia in general and to that of the newborn in particular. A number of new methods were also developed in its treatment. But the concept which is of fundamental importance to us today was that introduced by Little (1842, 1853, 1861), which suggested that the spasticities of childhood were the direct consequence of asphyxia at birth. This idea was lost sight of for a full century because of the overemphasis placed on focal hemorrhages caused by birth trauma, but recently it has been reintroduced by Courville and Marsh (1944), who pointed out the objective evidence in the very nature of the cerebral cortical lesions which emphasize their anoxial character. It has furthermore been suggested that some of the other less well-understood cortical degenerations of infancy and early childhood may have a similar genesis (Courville [1945]).

RESUSCITATION IN ASPHYXIA

If only the entire story of efforts at resuscitation of asphyxiated individuals could be known, what an interesting volume in the history of medicine it would be! Regrettably, we know so little of the early efforts in this direction. Indeed, there is but a single item antedating the sixteenth century which is known to the present writer. Garrison calls attention to the fact that in the Babylonian Talmud there is a statement to the effect that a newborn infant who failed to breathe was to be gently swung in a hammock in an effort to restore respiration. This fact seems to point the way that efforts at resuscitation were to take, for attention to therapeutic methods seems to be paramount.

Some sort of effort was almost certainly made to revive miners overtaken by noxious fumes while at their work or those suffocated by drowning; yet the literature prior to the eighteenth century is almost entirely silent on the subject. On the other hand, an early treatise on obstetrics by Pugh (1754) contained methods advocated to resuscitate infants who failed to breathe. From this time on a number of new methods were advocated. One of the first measures used was that known from Biblical times (2 Kings 4:33, 34)—mouth-to-mouth breathing—but whose more modern source is unknown. We find treatises on the subject in one of the earliest of obstetrical journals, the *Archiv fuer die Geburtshilft*, by Wegelin (1789-90) and by Löfler (1792). Monographs by Niemeier (1792), Freteau and Baudelocque ([1799] who advocated section of the umbilical cord), von Froriep and Schwarzot (1801), and Plenk (1807) also appeared about this time.

It would carry us too far afield to investigate thoroughly this subject of infant resuscitation; however, it is worth while to mention the method described by Marshall Hall (1856) which was destined to be quite extensively (and quite successfully) used in the middle decades of the nineteenth century. This method, which consisted of the alternate

hyperextension of the infant on one hand of the accoucheur and then flexion on the other, is still described in some English textbooks printed today. And with this manual method should be mentioned the swing method of Schultze now referred to only to be condemned. No doubt this measure has been effective in aggravating in many instances subdural hemorrhages which were responsible for the asphyxia in the first place.

To leave the history of this subject of resuscitation with only these few references to neonatal asphyxia would leave a considerable gap in our knowledge. We find that much instruction in both the prevention and relief of asphyxial states of other etiology in the literature of the eighteenth and nineteenth centuries and even before.*

To turn back to the eighteenth century, we find treatises on resuscitation by Welfroth (1725), Farkas (1762), and de Villiers (1771). Also about this time we have coming to light a series of books of instruction, often addressed to the public as a means of education dealing with the problem of "suspended animation" or "apparent death," as the asphyxial state was then called.† These manuals of instruction (or memorials) were published in Italy (at Firenze, 1772; by Tozzetti,‡ 1773 [figure 6]), in Germany (Munich, 1775), in France (de Gardanne, 1881, *a* and *b*), and in England (Hawes, 1782).

Still other monographs, given to a general consideration of the problem, included a section on therapeutics. Particularly noteworthy in this connection were the treatises of Goodwyn (1788) and of Plisson (1826), the latter containing an important section on the history of asphyxia.*

The scholarly essay by Kay (1834) may be considered to close the historical period on the therapy of asphyxial states. It is worth while, nonetheless, to note, in passing, those of our own day who have contributed so much to the treatment of anoxic states, viz., Barcroft (1925), Haldane, and associates in England, and Henderson (1924), Haggard (1923), and associates in the United States. To these must be added those (Fulton and associates) who have done so much to make flying in the stratosphere more safe. But this is getting out of the scope of this historical survey of the problem. As we write of either prevention of asphyxia or resuscitation we are brought face to face with a similar specter which has haunted the operating rooms for the past three quarters of a century. When its mask is torn off, we see that it too is asphyxia.

ANOXEMIA OF ANESTHESIA

The history of the anoxemic effects of the inhalation anesthetics is relatively short. It so happens that these effects were first noted in the case of nitrous oxide, whose identity was early recognized and whose anesthetic action was learned some time before its actual use in surgery. Oddly enough, nitrous oxide was first discovered by Priestley (1774) about the same time that he discovered oxygen. It was Sir Humphrey Davy (1800) who found that nitrous oxide, when inhaled, relieved pain, the discomfort of an erupting wisdom tooth being considerably alleviated. However, his

* An interesting item on the prevention of suffocation in infants is brought to light by Garrison (1937). He called attention to a placard published in the late thirteenth century warning parents not to take infants of less than three years of age to bed with them because of danger of suffocation. In the seventeenth century mothers sometimes deliberately overlay their infants to do away with them. Undoubtedly the old habit of "swaddling" infants with heavy clothing was also an occasional cause of suffocation.

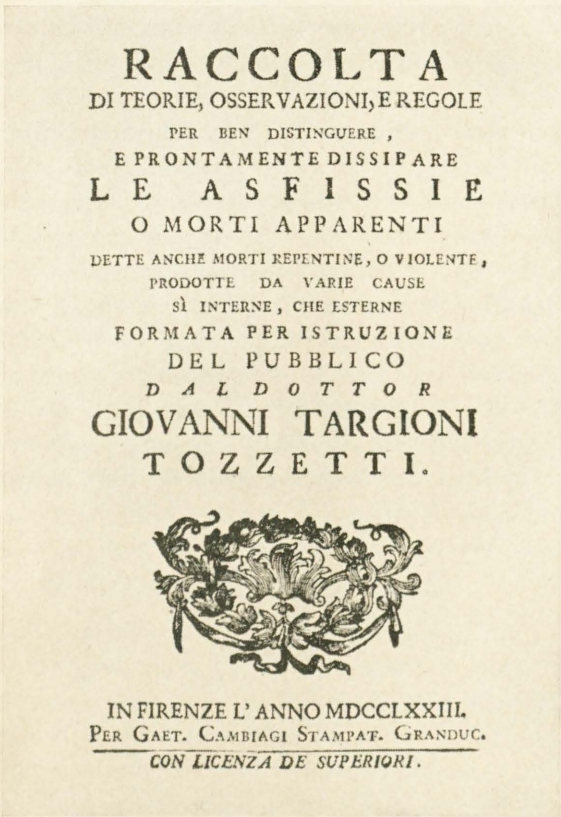
† It is worth while emphasizing the point recently made by Monge (1943) that the rulers of the ancient Incas forbade any mass migrations of captured tribes to altitudes other than those in which they were accustomed to live. It is presumed by Monge that this was done to prevent both the acute and chronic forms of "mountain sickness" which were so physically disabling. This seems to be an example of a prehistoric public health measure!

‡ A copy of this interesting and remarkable complete monograph has recently been added to the library of the Clinical Division of the College of Medical Evangelists through the gift of the Scripps-Remondino Library of Historical Medicine. This book gives considerable information on the history of asphyxia.

*As has already been implied, there are a number of treatises on suffocation or asphyxia, notably those of Schenk (1644), Bonet (1679), and of Tozzetti (1773), which contain valuable material of historical nature. This essay by Plisson and an undated one to appear about half a century later from the pen of Paul Bert are the only *specific* sources of historical material on this subject. (See figure six.)

suggestion that the gas might be used as an anesthetic in surgical operations, as well as the similar proposal by a young English surgeon, namely Hickman, went unheeded.

The first evidence of the noxious action of nitrous oxide was reported by Stanley (1842) when it was observed that the breathing of the crude gas (made by heating ammonium nitrate) for its exhilarating effects sometimes



RACCOLTA
DI TEORIE, OSSERVAZIONI, E REGOLE
PER BEN DISTINGUERE,
E PRONTAMENTE DISSIPARE
LE ASFISSIE
O MORTI APPARENTI
DETTE ANCHE MORTI REPENTINE, O VIOLENTE,
PRODOTTE DA VARIE CAUSE
SÌ INTERNE, CHE ESTERNE
FORMATA PER ISTRUZIONE
DEL PUBBLICO
DAL DOTTOR
GIOVANNI TARGIONI
TOZZETTI.

IN FIRENZE L' ANNO MDCCLXXIII.
PER GAET. CAMBIAGI STAMPAT. GRANDUC.
CON LICENZA DE SUPERIORI.

Fig. 6.—Title page of Tozzetti's monograph on asphyxia (or "apparent death") published in 1773. From copy in Scripps-Remondino historical collection.

resulted in forcible and uncontrollable muscular movements. After this gas came to be used as an anesthetic agent, the occasional occurrence of consequent convulsive seizures was reported by Warner (1882), Healy (1926), Evans (1928), and Clement (1928). It was soon suspected that these convulsive movements were the result of the anoxemia which was an invariable accompaniment of the use of nitrous oxide (Gardner [1902]; Wieland [1922]; Lake and Hertzmann [1924]; and Henderson [1927]).

Of greater interest in view of the cerebral effects of this anoxemia with nitrous oxide was the occurrence of residual manifestations in the form of psychic or psychoneurotic aberrations or rigidities, tremors, speech disturbances, etc. That these signs are due to physical damage to the cerebral cortex and basal ganglia, and that these lesions are the direct result of asphyxia has been proved beyond question (Courville [1936, 1938, 1939]; Lowenberg, Waggoner and Zbinden [1936]; Ford, Walshe, and Jarvis [1937]; O'Brien and Steegman [1938]).

Although not so evident in the case of the other inhalation anesthetics which are less likely to be accompanied by a serious degree of anoxemia, physical damage to the brain, of a similar character, has been shown after delayed death following other inhalation anesthetics. Even in the case of that old standby, ether, the convulsions which sometimes occur in the course of its administration are probably due to cortical anoxia (Courville, 1941).

* * *

And what of asphyxia consequent to exposure to the war gases? Or of those relative anoxemias associated with pulmonary diseases, notably pneumonia, cardiac diseases, and the anemias? Our understanding of these conditions is of recent vintage and of less concern to us in this short survey of the history of asphyxia. The literature dealing with these conditions will be cited in subsequent sections of this study.

But what of the intimate history dealing with the discovery of oxygen and carbon monoxide, the essential chemical fundamen-

tals of the problem, and what of the physical aspects of anoxemia? It has seemed more in order to discuss this phase of asphyxia with the physiology of normal and abnormal respiration to be considered in the following section of this essay. To this phase of the subject we will now give attention.

NOTE.—The bibliography will appear at the end of the completed article.

(To be continued)

CURRENT COMMENT

THE CIRCULATORY EFFECTS OF HISTAMINE*

FRED B. MOOR, M.D.

Few substances in the realm of biological chemistry have created more general interest than beta-iminazolylethylamine, commonly called histamine. It occurs in extracts of all animal and plant tissues, in which some is free and some results from protein cleavage. Its pharmacodynamics has been well elucidated, but its physiological significance is still largely theoretical. We are interested at this writing in the circulatory relationships of this interesting substance.

When applied locally by intracutaneous injection, by iontophoresis, or even by inunction, histamine produces a marked arteriolar and capillary dilatation with increased permeability of capillary walls and wheal formation. The wheal subsides in about half an hour, but redness and increase in skin temperature persist for a much longer period of time. It is also of interest to note that histamine applied by iontophoresis fails to produce marked local vasodilatation or wheal formation in areas where there is advanced occlusive vascular disease; in fact, this finding may be used as a measure of the circulatory impairment.

When a sufficient quantity of histamine gains access to the general circulation, as it may by subcutaneous, intramuscular, or intravenous injection, or by iontophoresis, systemic signs and symptoms arise, consisting of flushing of the face, a rise in skin temperature, a sharp drop in blood pressure, and a throbbing headache. Syncope occasionally occurs. With larger doses these signs and symptoms are all exaggerated, with the addition of bronchial constriction and dyspnea, vomiting and diarrhea. These manifestations are usually of short duration because of the rapid destruction of histamine, the compensatory increase in heart rate, and the sudden discharge of epinephrine, which is the specific physiological antagonist. In fact, this compensatory mechanism is so effective that a dilute solution of histamine given intravenously produces no marked change in the blood pressure.

On the physiological side Anrep *et al.* have demonstrated that histamine or a histamine-like substance is produced in muscle during exercise. These investigators considered histamine, by its vasodilating action, to be important in the physiological adjustment of the blood flow to the increased metabolic needs resulting from increased muscular activity. They also observed that a ten- to twenty-minute occlusion of the arterial blood supply to a limb caused a marked increase in the venous histamine level during the resulting reactive hyperemia. It appears, therefore, that histamine may have a definite physiological function to perform in augmenting the blood flow to meet local tissue requirements.

The recent report of Wirtschafter and Widmann on the treatment of the peripheral vascular diseases by the *in vivo* elaboration of histamine has added still further to the already widespread interest in this substance. After trying diethylether, with varying success, as recommended by Katz in the treat-

* From the Department of Therapeutics in the College of Medical Evangelists.

ment of these diseases, they reasoned that since Dale and Laidlaw had demonstrated that ether sensitized the capillaries to histamine, and since serum from some of their ether-treated patients produced cutaneous wheals and flares in nonallergic subjects and caused contraction of isolated guinea pig intestine, the favorable results in some patients might be due to the vasodilating action of histamine. From the work of Holtz they learned that the addition of ascorbic acid to histidine *in vitro* resulted in the production of histamine. By the simultaneous parenteral administration of large doses of histidine monohydrochloride and sodium ascorbate, Wirtschafter and Widmann were able to produce clinical improvement in eleven patients suffering from peripheral vascular disease, including seven with arteriosclerosis obliterans, two with thrombo-angiitis obliterans, and two with sudden arterial occlusion. They observed improvement of the peripheral circulation with relief of pain, increased warmth, and limitation of gangrene. Serum from these patients produced more marked cutaneous wheals and flares in nonallergic subjects than the serum from the ether-treated patients.

Although the ascorbic-histidine treatment of the peripheral vascular diseases is exceedingly interesting and appears physiologically sound, the present cost is prohibitive for many patients. If an adequate blood level of histamine is the only requisite for the successful treatment of these diseases, it seems that a simpler, easier, and cheaper method would be the administration of histamine itself by intravenous injection or by iontophoresis. By either of these latter routes any desired blood level could be maintained, although probably not as continuously as by the ascorbic-histidine procedure. Wirtschafter and Widmann have obviously made an important contribution to the therapy of the occlusive vascular diseases, which, as they have indicated, may be of value in the treatment of a number of other conditions in which the circulatory effects of histamine might be beneficial.

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INTRACRANIAL SURGERY*

WILLIAM T. GRANT, M.D.

DIAGNOSTIC METHODS

In the treatment of cerebral tumors there is still a great need for earlier diagnosis. It is surprising and disappointing to find a tumor that has grown into adjacent structures to such an extent that it cannot be completely removed and yet the demanding symptoms have lasted only a few weeks. One third of patients with a brain tumor have, as the initial symptom, spells which may be of mild or severe degree. Any patient who starts to have spells after the age of twenty-one years must be suspected of having a brain tumor unless some other abnormality can be clearly identified to account for the attacks.

After a careful history, physical and neurological examinations, X-rays of the skull are usually of interest. They should be taken so that the suspected side is shown stereoscopically and so that one anteroposterior view shows the pineal body. This structure is usually visible and can be measured for significant shift in the lateral view as well as in the anteroposterior.

When the electro-encephalogram fails to show an abnormal wave it can hardly help to locate the trouble, but a normal tracing does not in any way exclude the possibility of an area of pathologic change. When a normal tracing is found in the investigation of epilepsy it is possible to give metrazol intravenously during the tracing. This may bring on a typical spell or focal cortical discharges, and then there is a better chance that the electro-encephalogram will be of localizing value. This use of metrazol has not been standardized yet in cases of tumor.

Air studies can be carried out in two ways. For an encephalogram the air is introduced by spinal puncture, with the patient sitting. This does not always fill the ventricles completely, and, when looking for a tumor, a ventriculogram is more satisfactory, since the air is injected directly into the ventricle through a burr hole. The latter method is accompanied by less discomfort and less risk if intracranial pressure is increased. It must be remembered that a normal ventriculogram does not rule out a brain tumor. Thus it may be necessary to repeat the air study at intervals, depending on the clinical course.

When there is reason to expect an aneurysm or a vascular anomaly, a cerebral angiogram can be carried out by injecting the carotid artery in the neck with a radiopaque material and taking X-rays at the proper time. Thorotrast or diodrast is used, and one may puncture the artery under direct vision or by blind puncture. From two to five films are then exposed at intervals of about one second. A mechanical film changer has been developed that makes the exposure automatically as the cassettes are pulled to one side. Some types of tumor can be shown in this way better than by air studies.

Neurophysiological methods are gradually being adapted to aid in the neurological examination. Quantitative and graphic records allow a more exact evaluation of the function being tested and also an analysis that is not possible when the response is simply observed visually (figure 1).

* From the Department of Nervous Diseases (Neurosurgery), College of Medical Evangelists, Los Angeles, California.

SURGICAL PROBLEMS

The risk of an operation on the brain is not great so that, except in cases of large tumor with irreversible changes in the brain stem, the chance of survival is quite good. A patient is less upset by the wide excision of a brain tumor with surrounding brain than he is by a partial removal. Postoperative hyperthermia, once the bugbear of neurosurgeons, is seldom seen any more. It is due to diffuse cerebral edema that develops when a high intracranial pressure is allowed to drop too far or too quickly. To avoid this, the ventricular pressure is allowed to fall by stages before the air study is carried out. The use of hypertonic sucrose before and after operation helps in addition to prevent cerebral edema.

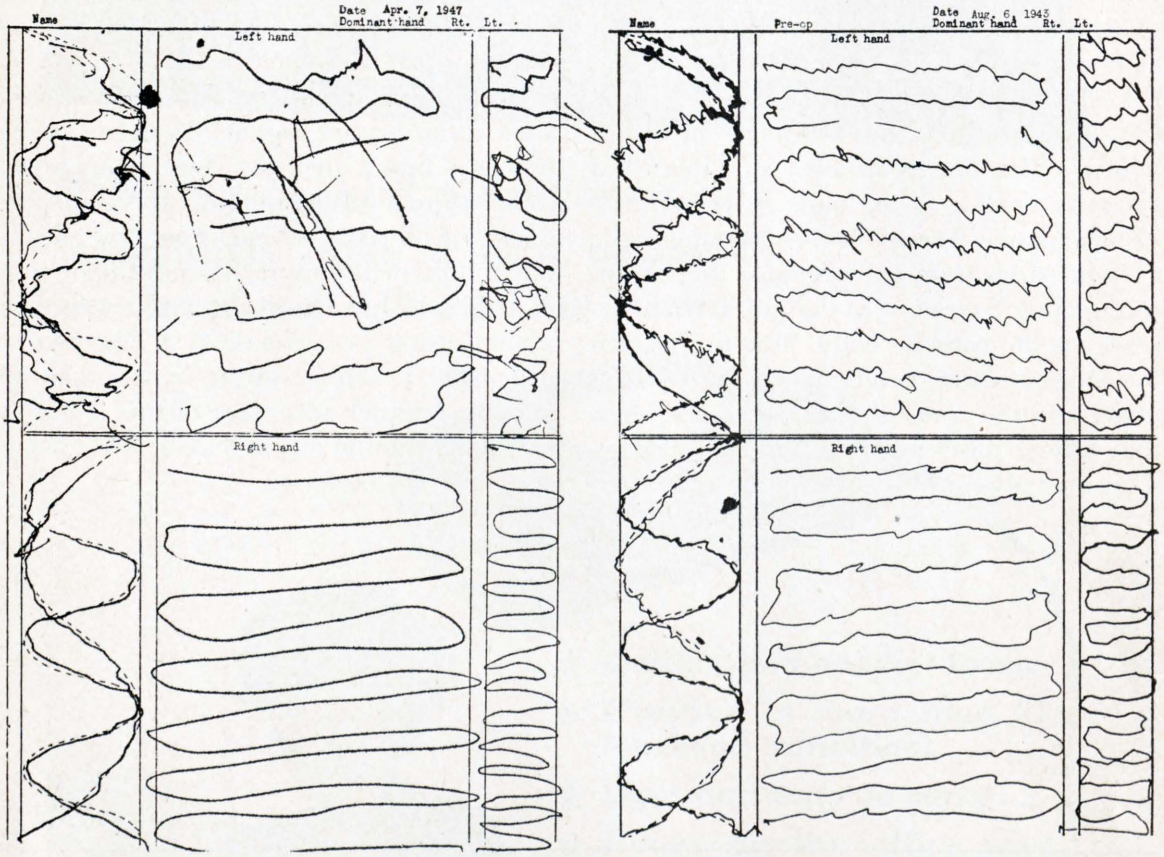

FIG. 1. The two wavy tracings above were made with a flexible pen, and serve to record motor control similar to that in the finger-to-nose test. The method* was described in detail recently. The tracing on the left shows much disability of the left hand, due to an old injury in the right cerebral hemisphere. The gross and irregular deviations from the intended line of movement are typical of a lesion affecting the precentral gyrus. The other tracing was made by a patient with a left cerebellar lesion. The characteristic effect is a tremor that is evident in all parts of the tracing. Even in very severe cases the general line of movement is surprisingly good, in contrast to the tracings made by patients with lesions in the cerebral hemisphere.

When the scalp has been infiltrated with novocaine the operation is almost painless, and light anesthesia with avertin or sodium pentothal, or both, is sufficient. In cases with

* Grant, W. T.: Graphic methods in the neurological examination. Wavy tracings to record motor control, Bull. Los Angeles Neurol. Soc., 12, 1947 (in press).

compression of the medullary centers an intratracheal tube is necessary for possible artificial respiration, and this calls for a deeper level of anesthesia. Often a good part of the operation can be carried out under local anesthetic and the patient does not ask to go to sleep until he becomes tired or until irritation of the dura causes too much discomfort.

Measures to stop bleeding vessels have been extended beyond the use of silver clips and the electrocautery. The latter is still applicable in most places and, when an important structure lies directly beneath, one can avoid excessive heating of the underlying brain by using a bipolar forceps. In this instrument the current passes from one prong of the forceps to the other instead of to the indifferent electrode via the patient's body. Vitamin K given for one or two days before operation improves materially the clotting time. It is not often that a large vessel is torn, since improved instruments allow the vessels to be cauterized under direct vision before being divided. Such instruments include self-retaining retractors with attached suction, irrigation and lights, insulated cautery tips and forceps so that they can be used at the bottom of a deep hole without being short-circuited at the side of the wound. Fibrin foam and the fabricated gelatin products are most useful to stop bleeding from veins that enter one of the large venous sinuses.

Deep X-ray treatment is usually of value after an infiltrating tumor has been removed from the brain. In many cases of apparently complete removal of a glioma there are small islands of cells left behind. The most effective way to deal with any remaining tumor tissue is to give X-ray treatment directly into the wound, using a contact tube. A dose of more than 6000 r. can be given in less than one minute. Another advantage of this is that the patient avoids the loss of hair that follows the postoperative radiation.

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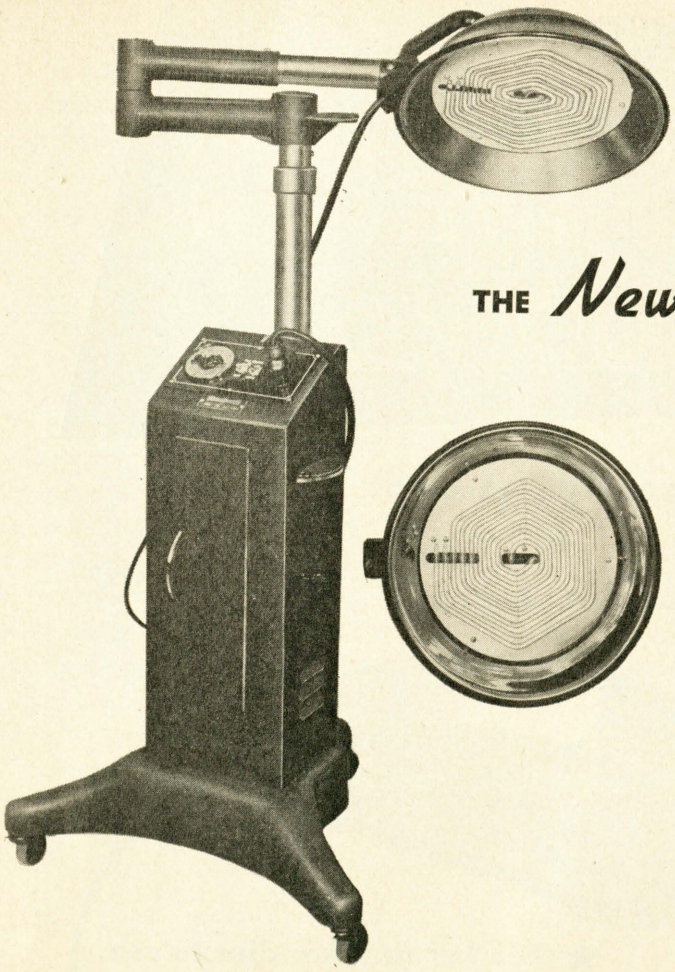

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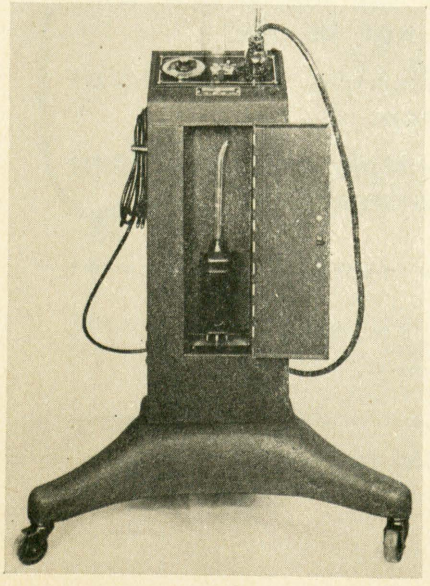

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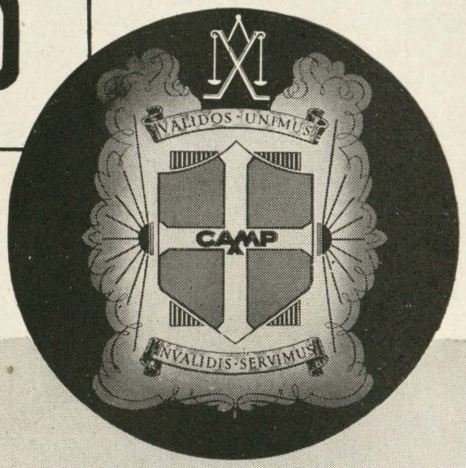

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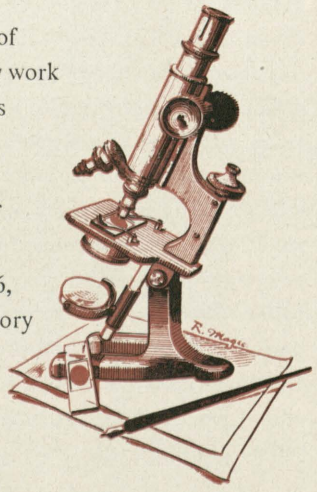

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